CPMA
COLOR PIGMENTS
MANUFACTURERS
ASSOCIATION, INC.

May 15, 1998

Dr. C. W. Jameson
National Toxicology Program
Report on Carcinogens
MD EC-14
P.O. Box 12233
Research Triangle Park, NC 27709

Re: National Toxicology Program; Call For Public Comments, Listing In The Report of Carcinogens, Ninth Edition

Dear Dr. Jameson,

I am writing on behalf of the Color Pigments Manufacturers Association, Inc. ("CPMA"). The CPMA, formerly DCMA -- the Dry Color Manufacturers' Association, is an industry trade association representing color pigment companies in Canada, Mexico, and the United States. CPMA represents small, medium and large color pigment manufacturers throughout Canada, Mexico and the United States, accounting for 95% of the production of color pigments in North America.

Color pigments are widely used in product compositions of all kinds, including paints, inks, plastics, glass, synthetic fibers, ceramics, colored cement products, textiles, cosmetics, and artists' colors. Color pigment manufacturers located in other countries with sales in Canada, Mexico, and the United States, and suppliers of intermediates to the color pigment industry are also members of the association.

We are writing in response to the National Toxicology Program ("NTP"), notice published in the Federal Register March 19, 1998. The Notice, 63 Fed. Reg. 13418 indicated that NTP was taking final comments on a proposed change in the carcinogenicity classification for all cadmium compounds to that of "Known Carcinogen". The CPMA objects to this classification as it will apply to cadmium pigments.

Cadmium pigments are included in this classification even though there is no clear evidence from which to conclude that cadmium pigments are carcinogenic. All available evidence, involving animal experiments, indicates that cadmium pigments do not provide sufficient bioavailable cadmium to induce a carcinogenic response.

Cadmium pigments are highly insoluble compounds of cadmium used as colorants for artist's colors, specialty paints and inks, plastics, and aerospace coatings. These pigments all exist in a highly stable hexagonal crystal form and are classified as cadmium zinc sulfide, Color Index ("C. I.") Pigment Yellow 35, cadmium sulfide, C. I. Pigment Yellow 37, cadmium sulfoselenide, C. I. Pigment Orange 20 and cadmium selenide, C.I. Pigment Red 108. Like many other calcined inorganic compounds, the crystal structure of cadmium pigments imparts a stability which distinguishes these products from other cadmium compounds. As we understand it, the NTP is acting to reclassify cadmium compounds as a follow up to action recently taken by the International Agency for Research on Cancer ("IARC").

Although cadmium pigments are included in the IARC classification of cadmium in all forms, the classification is based on chronic inhalation studies involving other more soluble cadmium compounds. Two chronic animal inhalation studies involving cadmium pigments have been reported. In the first, mice and hamsters were exposed to cadmium pigment at concentrations up to 1,000 micrograms per cubic meter of air (as Cd) for 44 weeks. No carcinogenic response was observed in the experiment. [1] In the second long-term inhalation study, rats were exposed to pigment at airborne concentrations up to 2,430 micrograms per cubic

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[1] Heinrich, U., et al. "Long-term Inhalation Exposure of Syrian Golden Hamsters and NMRI Mice to Various Cadmium Compounds," presented at the 4th IUPAC Cadmium Workshop, Schmallenburg-Graftschaft, Germany, September 11-13, 1988.

meter of air for up to 18 months. [2] These authors, for the first time, reported a carcinogenic response similar to the other more soluble cadmium compounds tested. This response was noted at very high dose levels far greater than that used for other cadmium compounds. Subsequent investigations by the original authors and others determined that the aerosol method used to expose the animals to cadmium pigment caused the cadmium pigment to breakdown into other, soluble, cadmium compounds. [3 4 5] Indeed, the original findings of the Glaser, et al. study can be entirely explained by the inadvertent exposure the animals received from other soluble forms of cadmium. [6]

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[2] Glaser, U. et al. "Carcinogenicity and Toxicity of Four Cadmium Compounds Inhaled by Rats", presented at the 4th IUPAC Cadmium Workshop, Schmallenburg-Graftschaft, Germany, September 11-13, 1988.

[3] Glaser, U. et al. "Cadmium Solubility in Suspensions During Long-Term Generation of Cadmium Sulfide Aerosols", presented at the Toxic Metal Compounds Workshop, Les Diablerets, Switzerland, March 1991.

[4] Konig, H.P. et al., "How does the solubility of cadmium sulfide (CdS) affect the results of inhalation studies with CdS particles?" Presented at 3rd European Meeting of Environmental Hygiene, Düsseldorf, F.R.G., June 1991.

[5] Gagliardi, G. B. and Ulicny, L. J., "Photodecomposition of Dilute Cadmium Sulfide Slurries," presented at the XXIVth RETEC, Charlotte, North Carolina, October 1990.

[6] Ulicny, L. J. "What is the Evidence for the Carcinogenicity of Cadmium Sulfide Pigments?", presented at the 7th International Cadmium Conference, New Orleans. Louisiana, April 1992.

The proposed "blanket" classification of cadmium compounds by the US NTP contrasts strongly with the situation inside the European Community. Its chemical hazard classification system recognizes three levels of hazard from cadmium compounds:

Hazard Classification & Materials Affected	**Risk & Safety Phrases Required**
TOXIC: cadmium oxide cadmium sulphate cadmium sulphide (chemical) cadmium chloride	• May cause cancer by inhalation. • Harmful if swallowed. • Toxic: danger of serious damage to health by prolonged exposure through inhalation and if swallowed. • Avoid exposure - obtain special instructions before use. • In case of accident or if you feel unwell, seek medical advice (show label where possible).
HARMFUL: All other cadmium compounds EXCEPT cadmium pigments.	• Harmful by inhalation, in contact with skin and if swallowed. • Do not breathe dust.
CADMIUM PIGMENTS	• NO statutory risk or safety phrases required. Self-classify material on the basis of its physical and chemical properties. • This self-classification leads to a "non-hazardous" result. All manufacturers do, however, use a voluntary "good practice" label including e.g. "do not breathe dust", as this should not be done with any chemical.

With respect to human studies involving carcinogenicity and cadmium sulfide generally, there are also new studies which cast doubt on the assumption that cadmium sulfide (or therefore, cadmium pigments which are far more stable) is a carcinogen. In one study, the authors concluded:

> "Conclusions-Hypotheses which are consistent with the study findings include: (a) cadmium oxide is the presence of arsenic trioxide is a human carcinogen, (b) cadmium oxide and arsenic trioxide are human lung carcinogens and cadmium sulphate and cadmium sulphide are not (or they are less potent carcinogens), or (c) arsenic trioxide is a human lung carcinogen and cadmium oxide, cadmium sulphate, and cadmium sulphide are not." [7]

The authors in this study were re-examining the data reviewed by Dr. Thun in the landmark study used by many organizations to establish the carcinogenicity of all cadmium compounds. [8] Certainly this additional data calls the assumed carcinogenicity for cadmium pigments into question. Long-term health studies of workers at cadmium pigment manufacturers have failed to show any evidence of carcinogenic activity from exposure to cadmium pigments alone. Positive effects were only seen when there was also exposure to cadmium oxide, known for decades to be a highly-toxic material. These groups of workers, with much greater (certainly in

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[7] Sorahan, T., Lancashire, R.J., "Lung Cancer Mortality in a Cohort of Workers Employed at a Cadmium Recovery Plant in the United States: An Analysis with Detailed Job Histories", Occ. Env. Med. 54, pp. 194-201 (1997)

[8] Thun, M. et al. "Mortality Among a Cohort of US Cadmium Production Workers - An Update", J. Natl. Cancer Inst. 1985; 76, p. 825

the past) and more prolonged exposure than end-users of cadmium pigments, would be expected to show a clear positive effect if cadmium pigments had carcinogenic activity.

Additionally, cadmium pigments have been used by artists and industry for decades. If there were a discernible link between lung cancer and the use of cadmium pigments, evidence of that linkage would have been reported or known.

Cadmium pigments are important colorants which produce a unique, long-lasting, brilliant, light and heat stable, yellow to red color in the resins or coating matrix in which these colors are used. Cadmium pigments are unsurpassed in many high temperature plastic, ceramic and outdoor applications. By simply assuming, without evidence, that these valuable compounds are carcinogenic, NTP seriously harms and unnecessarily alarms the markets and users of these valuable products.

We hope this information is helpful to you in reviewing the overbroad classification of cadmium compounds which now includes cadmium pigments. Please call if we can be of further assistance.

Sincerely,

J. Lawrence Robinson
President